REMARKS

In the Claims:

Claims 3, 5-7, and 23-25 are pending.

Claims 3 and 24 are amended herein. No new matter is added by this amendment and support for the amendment may be found throughout the specification, including at paragraphs 0002, 0005, 0017, 0024, 0025, 0032, 0033, Table 1 on page 6 and original claims 10, 12, 15, and 18.

To expedite prosecution, claim 5 is cancelled herein without disclaimer or prejudice to pursuing the invention of claim 5 in continuing applications.

Claim Rejections:

35 U.S.C. § 112, ¶ 1:

Claims 3, 5-7, and 23-25 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Office action alleges that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors were in possession of the claimed invention, because the phrase "a standardized concentration of the marker compound that is used to prepare an extract . . ." as present in claims 3 and 24 is alleged to be new matter. Specifically, the Office action alleges that the phrase is considered New matter because "there is nowhere in the specification which teaches that the maturation stage *is selected* with a standardized concentration of the marker compound." (Office action dated July 10, 2008, p. 3).

Applicants respectfully note that claim 5 has been cancelled without disclaimer or prejudice and therefore, this ground of rejection as to claim 5 is overcome. Applicants respectfully request it be withdrawn.

Applicants respectfully disagree with this ground of rejection as it pertains to the remaining claims. One of ordinary skill in the art would know the metes and bounds of a standardized concentration of marker compound. According to Section 2173.05(b) of the MPEP, that alone is sufficient: the "[a]cceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification."

More specifically, standardization of extracts has a well-understood meaning. A standardized concentration of a marker compound merely means that each extract having a standardized concentration of a marker compound has the same concentration of that marker compound. Thus, for standardization, the important aspect is that the ***level of marker compound remains consistent*** from extract to extract.

Plant extracts for pharmaceutical and medicinal purposes are commonly standardized as a means of ensuring uniformity. Paragraph 0025 of the specification explains, "standardization to a marker such as chicoric acid is important to meet market or regulatory expectations." Standardization ensures that each herbal extract contains equal amounts of the marker compound. Furthermore, standardization provides for uniformity in extracts from a single provider, such as the present Assignee, Access Business Group International.

The present application provides an example that describes using chicoric acid as a marker compound for an *Echinacea* extract and thereby illustrates the principle that each preparation of *Echinacea* extract must have the same concentration of marker compound. Specifically, Table 1 and paragraphs 0022 and 0024 of the specification report that levels of chicoric acid do not vary greatly from plant to plant at maturation stages 1 through 6. For instance, the values reported in Table 1 range from 3.49 ± 0.09% to 3.54 ± 0.14% for maturation stages 1 through 6. As stated in paragraph 24, the variations are within levels generally accepted by those skilled in the art. Hence, based on this teaching, one of ordinary skill in the art would appreciate that a standardized concentration

of the marker compound chicoric acid would fall in the range of 3.49 ± 0.09% to 3.54 ± 0.14%.

Applicant respectfully disagrees with the statement in the Office action that "[t]he natural content of the chicoric acid is not considered 'standardization.'" (Office action dated July 10, 2008, p.3). As used in the specification, "standardized" refers to a useful industry measurement wherein suppliers insure that each extract has the same level of a marker compound. The specific level is less important than that each extract have the same level of marker compound. Indeed, the standardized concentration of a marker compound may even be a concentration that occurs in nature if all extracts from one supplier have that level or a supplier may standardize to an artificial amount of a marker compound. Regarding the example, selecting an *Echinacea* plant at any maturation stage between 1 and 6 will inherently have the **same** concentration of chicoric acid, *i.e.*, a standardized level of chicoric acid. Therefore, one of ordinary skill in the art, in view of the specification, will understand what is claimed by "standardized concentration of the marker compound." This ground of rejection is overcome and Applicants respectfully request that it be withdrawn.

35 U.S.C. § 103(a)

Claims 3, 5-7 and 24 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over A in view of C in view of E or B in view of C in view of E, wherein A = Seidler-Lozykowska et al. (2003), B = Dou et al. (2001 – Abstract), C = Rininger et al. (2000) and E = Gahler et al. (US 6,511,683). This new rejection was put in place "in the event that Applicants specifically amend claim 3 or 25 to include specifically that the marker compound is chicoric acid." (Office action dated July 10, 2008, p.4)

Claims 3, 5-7 and 24 are also newly rejected under 35 U.S.C. 103(a) as being unpatentable over A in view of C in view of D in view of E or B in view of C in view of D in view of E, wherein A, B, C and E remain the same, and D = Wyllie et al. (US 2003/0235890). This new rejection was put in place "in the event that

Applicants specifically amend claim 3 or 25 to include specifically that the marker compound is chlorogenic acid. (Office action dated July 10, 2008, p.8).

At the outset, Applicants respectfully note that claim 5 has been cancelled without disclaimer or prejudice and therefore, this ground of rejection as to claim 5 is overcome. Applicants respectfully request it be withdrawn.

Applicants respectfully disagree with these grounds of rejection pertaining to the remaining claims. According to Section 2141 of the MPEP, which is consistent with the Supreme Court's recent decision in *KSR Int'l Co. v. Teleflex Inc.*, 82 USPQ 2d 1385 (U.S. 2007), when determining whether a claimed invention is obvious under 35 U.S.C. § 103, the following tenets of patent law must be adhered to:

> (A) The claimed invention must be considered as a whole;
>
> (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;
>
> (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and
>
> (D) Reasonable expectation of success is the standard with which obviousness is determined.

Hodosh v. Block Drug Co., 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986).

When these tenets of patent law are properly applied, it is clear that the claimed invention is not obvious in view of the cited references.

First, the claimed invention as a whole is a method for determining optimal harvest window of *Echinacea* based on selecting a plant maturation stage that has both a standardized concentration of a either chicoric acid or chlorogenic acid and immunostimulatory activity. The claimed method also includes a step of preparing a standardized extract at that selected maturation stage.

The cited references as a whole do not teach this method; in fact they teach away from using the two specific marker compounds chicoric acid or chlorogenic acid. Two of the cited references, Seidler-Lozykowska and Dou, examine when the greatest levels of typical marker compounds used to standardize extracts may be obtained and from which specific parts of the plant they may be obtained. Neither Seidler-Lozykowska nor Dou discuss any immunopotentiating activity of *Echinacea*. Two of the other cited references, Rininger and Gahler, teach that standardized extracts using chlorogenic acid or chicoric acid as marker compounds do not exhibit immunostimulatory activity.

Rininger analyzed whether extracts standardized to a 4% concentration of phenolic marker compound exhibited immunopotentiating activity. Rininger clearly teaches that the analyzed ***standardized*** extracts were "***inactive***" for immunostimulatory activity. *See* Rininger at 8, 10. Furthermore, Rininger specifically analyzed chlorogenic acid and chicoric acid. Rininger teaches that *Echinacea* extracts that were ***standardized*** with either chlorogenic acid or chicoric acid as marker compounds were ***not*** found to possess any immunostimulatory activity. *Id.* Indeed, Rininger teaches, "standardized *Echinacea* extracts as well as purified chemical standards for the production of *Echinacea* extracts were found to be inactive for these immunomodulatory functions." *Id.* at 10. This teaching is consistent with Rininger's analysis of ***non-standardized*** extracts. Specifically, Rininger analyzed ***non-standardized*** *Echinacea* extracts and found that the ***non-standardized*** extracts possessed immunostimulatory activity. *Id.* at 7-8. Thus, one of ordinary skill in the art may fairly conclude from these teachings of Rininger that non-standardized extracts have immunostimulatory activity, but standardized *Echinacea* extracts do not possess immunostimulatory activity, particularly *Echinacea* extracts standardized with chlorogenic acid or chicoric acid as the marker compound.

Gahler did recognize the need and advantage of standardizing *Echinacea* extracts using marker compounds to obtain an extract with optimized medicinal potential. Gahler also recognized that *Echinacea* must be harvested at various

times. Gahler, however, teaches that using any marker compound alone, and specifically chicoric acid alone, will result in no immunostimulatory activity. Specifically, Gahler teaches that immune enhancing activity is only observed when a number of marker compounds are used in combination with each other; for example, Gahler teaches that using chicoric acid, alkylamides and polysaccharides together as marker compounds enhances macrophage phagocytic activity and TNF-α production. (Col. 16, ll. 37-61). But, Gahler goes on to teach that an *Echinacea* extracts standardized with primarily chicoric acid as the marker compound or polysaccharides as the marker compound do not display immunostimulatory activity. (Col. 24, ll. 29-38). Specifically, Gahler states, "Echinacea cichoric acid extract of the invention . . . had no significant effect on the phagocytic activity or the phagocytic index of rat alveolar macrophages. . . . Similarly . . . an *Echinacea* polysaccharide extract of the invention . . . had no significant effect on the phagocytic activity or the phagocytic index of rat alveolar macrophages." *Id.* Gahler further teaches that "Echinacea cichoric acid and polysaccharide extracts . . . did not significantly increase the level of nitric oxide production by alveolar macrophages." (Col. 24, ll. 64-67). Furthermore, Gahler explains, "Echinacea cichoric acid extract . . . did not significantly increase the level of TNF-α production by alveolar macrophages." (Col. 25, ll. 15-18). Neither did *Echinacea* chicoric acid extracts or polysaccharide extracts "cause a significant increase in IFN-γ production by the splenocytes" (Col. 25, ll. 35-37), nor did they "affect the production of IL-2 in splenocytes." (Col. 26, ll. 4-7). Thus, one of ordinary skill in the art would understand from Gahler that some *Echinacea* extracts standardized by multiple marker compounds can be harvested at certain maturation stages to optimize immunostimulatory activity, but that *Echinacea* extracts standardized with only one marker compound, particularly with only chicoric acid, will show ***no immunostimulatory activity***.

Applicants respectfully submit that when the claims are considered in their entirety and when the references also are considered as a whole, without relying

on impermissible hindsight, it is clear that the cited references do not provide any reasonable expectation of success in formulating a method for determining optimal harvest window of *Echinacea*, based on selecting a plant maturation stage that has both a standardized concentration of either chicoric acid or chlorogenic acid as a marker compound that is obtained from the preparation of *Echinacea* plant for preparing a standardized extract, and that has immunostimulatory activity. Specifically, Seidler-Lozykowska and Dou both teach means for producing *Echinacea* extracts with the highest concentration of compounds used to standardize *Echinacea* extracts. Rininger teaches that neither standardized *Echinacea* extracts nor the common marker compounds used for standardization—particularly chlorogenic acid and chicoric acid—exhibit immunostimulatory activity. Gahler teaches that standardized extracts using multiple marker compounds in combination can produce immunostimulatory activity, but Gahler specifically teaches away from using only one marker compound to standardize the extracts, and particularly teaches that *Echinacea* extracts standardized using chicoric acid do not have immunostimulatory activity. Thus, one of skill in the art would not, based on the teaches of the cited references, expect the claimed method of optimizing harvest window of the *Echinacea* plant by selecting a plant maturation stage that has a standardized concentration of either chicoric acid or chlorogenic acid, yet also maintains immunostimulatory activity, to be successful.

Claims 3, 6-7, and 23-25 are not obviousness in view of the cited references. Applicants have overcome these grounds of rejection and respectfully request that they be withdrawn.

CONCLUSION

Applicant believes that currently pending claims 3, 6-7, and 23-25 are patentable. The Examiner is invited to contact the undersigned attorney for Applicant via telephone if such communication would expedite allowance of this application.

Respectfully submitted,

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